

Brief communication

Basal cell skin cancer and the risk of second primary cancers: a cancer registry–based study in Lithuania



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ABSTRACT

Purpose: The aim of this population-based cohort study was to determine the risk of second primary cancer in basal cell carcinoma (BCC) patients in Lithuania.

Methods: This analysis was based on patients diagnosed with BCC in Lithuania between 1998 and 2007 and followed until 2011. Standardized incidence ratios for subsequent cancers as a ratio of observed number of cancer cases in people with previous BCC diagnosis to the expected number of cancer cases in the underlying general population were calculated.

Results: After diagnosis of BCC, 1442 new cases of selected cancers were diagnosed. Compared with the general population, the incidence of all new primaries combined after BCC was very close to expected. Statistically meaningful increase in developing subsequent cancer was obtained for Hodgkin's lymphoma, prostate cancer, and leukemia in men, and for cancers of the lip, lung, and breast in women. Risk of melanoma and thyroid cancer was significantly elevated in both sexes. Relative risk of cancer of the eye was increased although not significant.

Conclusions: In our study, we found increased cancer risk for cancers related to sun exposure. In addition, increased risks were identified for Hodgkin's lymphoma, thyroid cancer, leukemia, prostate, and breast cancer in BCC patients.

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Introduction

Ultraviolet (UV) irradiation is considered to be the most important risk factor for the development of skin cancer [1]. Both prolonged cumulative exposure and intermittent exposure to high levels of UV radiation in occupational as well as nonoccupational settings are responsible for the development of basal cell carcinoma (BCC) [2–4]. A number of registry-based epidemiologic studies have reported an increased risk of several second primary cancers after an initial diagnosis of BCC [5–9].

BCC is a predominant form of skin cancer that is locally aggressive, grows slowly and rarely metastasizes, and the removal of the tumor is an effective treatment method. Therefore, the influence of treatment of BCC for development of second primary cancers is unlikely, and the observed risk should be attributed to some shared external and/or internal risk factors.

A systematic review on the risk of second primary cancers after nonmelanoma skin cancer by Wheless et al. showed that personal history of skin BCC is associated with an increased risk of

developing other malignancies [8]. Increased risk of melanoma, lip, and other skin cancers after an initial diagnosis of BCC is likely related to long-term sun exposure. In addition, several unexplained associations with BCC were identified as well, such as an increased risk of lung, mouth, and pharynx, thyroid cancer, and non-Hodgkin lymphoma (NHL). Some authors suggested that the apparent absence of any single environmental agent that could explain the multiple cancer risk indicates that the association between skin cancers and risk of other malignancies might be explained by other mechanisms, such as immunosuppression, chronic inflammation, variation in DNA repair efficiency, and that diagnosis of skin cancer may be a marker of a general high cancer-risk phenotype [8,10]. Several recent studies suggested a possible inverse relationship between UV exposure and risk of colon, breast and prostate cancer and some other solid cancers [7,11,12]. However, difficulties in interpretation of such data have been recently discussed [13].

The aim of this population-based cohort study was to determine the risk of second primary cancer in BCC patients in Lithuania.

Materials and methods

Data for our study were extracted from Lithuanian Cancer Registry which is a nationwide population-based cancer registry that

The authors declare that they have no conflict of interest.

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contains personal and demographic information, as well as information on diagnosis of all people diagnosed with cancer in Lithuania since 1978 [14]. The patients' vital status is available from 1990. The principal sources of information on cancer cases are primary, secondary, and tertiary health care institutions. These data are supplemented with automatically extracted reports from some pathology laboratories.

This analysis was based on BCC diagnosed in Lithuania between 1998 and 2007. Only patients with their first primary cancer diagnosed in this period were included. Identification steps for constructing the cohort for this study are shown in Figure 1. The cases were identified from the Cancer Registry-based on the *International Classification of Diseases, Tenth Revision* (ICD-10) code C44, as well as the *International Classification of Diseases for Oncology, Third Edition* (ICD-O-3) morphology code 809. In total, 12584 patients with first primary cancer of morphologically verified BCC were examined and followed till December 31, 2011, date of death, date of lost to follow-up, or date of diagnosis of second primary cancer, whichever came first.

National rule for multiple cases of BCC registration has changed several times in Lithuania. Between 1996 and 2008, every new BCC case arising more than 5 years after the previous BCC diagnosis was registered as multiple primaries. Since 2009, only one BCC case is accepted per patient. Owing to changes in the registration practice,

we did not analyze the risk of second primary nonmelanoma skin tumors.

We calculated standardized incidence ratios (SIRs) for subsequent cancers as a ratio of observed number of cancer cases in people with previous BCC diagnosis to the expected number of cancer cases in the underlying general population. Expected numbers were calculated as multiplication of the exact person-years under observation in the cohort by sex-, year-, and 5-year-age-group-specific national incidence rates. Ninety-five percent confidence intervals for the SIRs were estimated assuming number of observed cancer cases follows Poisson distribution.

Results

Table 1 lists observed number of cases and SIRs of developing second primary cancer together with 95% confidence intervals for selected cancer sites calculated for both sexes combined, as well as for men and women separately. In total, 4510 men and 8074 women had BCC as their primary diagnosis between 1998 and 2007, and 1442 new cases of selected cancers were diagnosed (781 in men and 661 in women) within a period of 14 years. Prostate cancer was the most common second primary cancer and consisted almost 40% of all new cancer diagnosis in men; however, this large number of

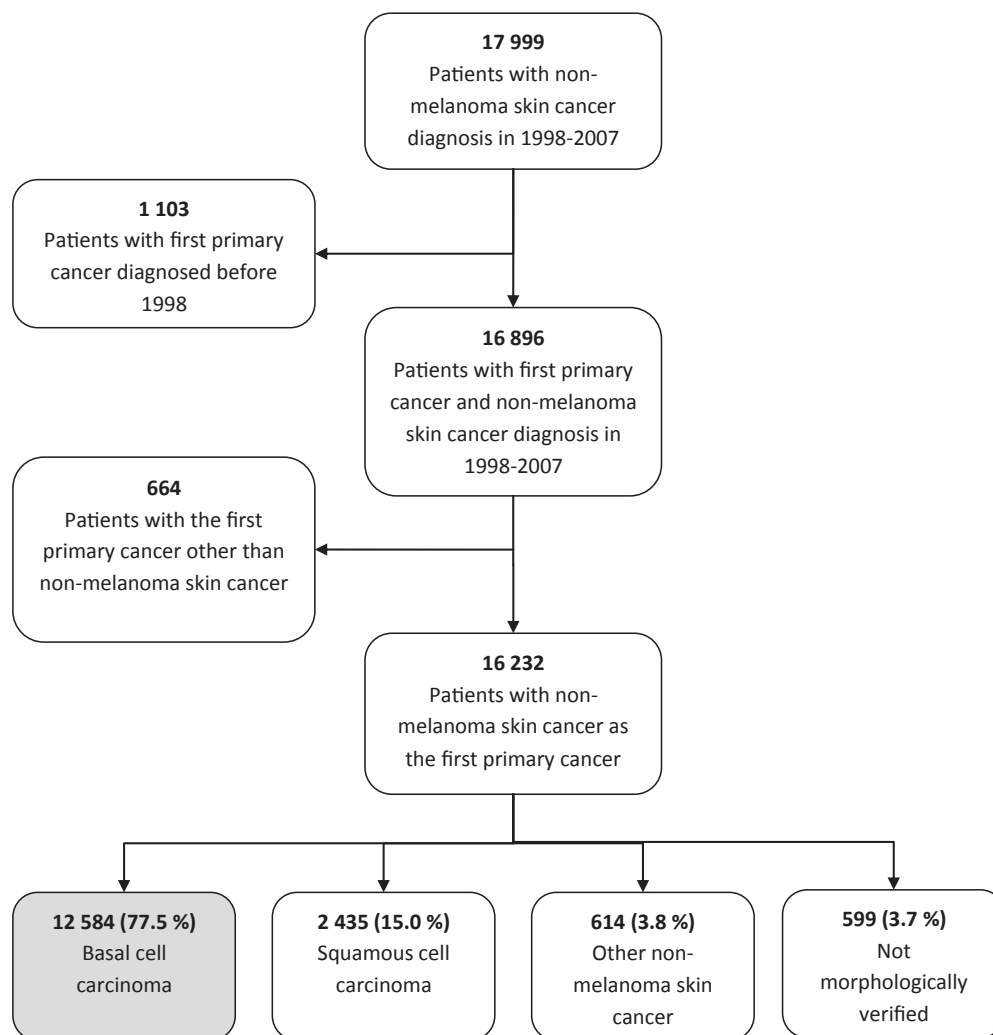


Fig. 1. Study design steps for constructing a cohort of patients with the BCC in Lithuania between 1998 and 2007.

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